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(54) DERMATIC AGENT FOR EXTERNAL USE

(57)Abstract:

PURPOSE: To obtain a dermatic agent for external use having synergistically improved anti-inflammatory action of kojic acid or its derivative and effective to promote the development of the skin-whitening effect by using kojic acid and/or kojic acid derivative in combination with extract of a specific plant.

CONSTITUTION: This dermatic agent for external use contains (A) kojic acid and/or its derivative and (B) one or more kinds of extracts of plants selected from Iceland moss, iris, oak bark, fumitory, gardenia, candock, eyebright, Japanese linden, field horsetail, mistletoe, common mallow, herb bennet, dried orange peel, daisy, elm, grape, soapberry, melilot, cornflower and creeping saxifrage.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Industrial Application]Are it the skin external preparations by which it is characterized that this invention contains kojic acid and/or its derivative, and the extract of specific vegetation as an active principle, and in more detail, While raising synergistically the anti-inflammatory activity of kojic acid or its derivative by using the extract of specific vegetation together, it is related with the skin external preparations which brought the manifestation of the fair operation forward.

[0002]

[Description of the Prior Art]It is known that spots, such as a stain, a freckle, etc. which appear on the human skin, will mainly be brought about by deposition of YUUMERANIN. Generation of melanin used as such a stain and a cause of a freckle is controlled, and also research of various kinds of cosmetics aiming at the milky skin of the whole skin is also done for many years. Although to blend hydrogen peroxide and peroxides, such as zinc perborate, with cosmetics, to blend vitamin C, cystein, colloidal sulphur, etc. into cosmetics, etc. were tried as those examples, what should satisfy all in respect of preservability or a fair effect is not obtained.

[0003]As a factor which this invention persons removed spots, such as a stain, a freckle, etc. which appear in the human skin, have repeated the research on the external preparations for raising a fair operation of the whole skin over many years, and participates in the color of normal Homo sapiens's skin, Although there are melanin, the amount of carotene, a blood stream (oxidation, reduced hemoglobin), and the thickness and transparency of the skin, and lights are reflected, absorbed and scattered about by these factors and become color [of the skin], It solved that it was a factor of the pigmentation with melanin, especially mainly biggest brown and black YUUMERANIN in these, and has groped for the substance which controls generation of this melanin. In the research, kojic acid (5-oxy-2-oxymethyl gamma-pyrone) and

its derivative find out that the extremely outstanding melanin generation depressant action is shown, the fair cosmetics and external preparations which make these an active principle were invented (JP,56-18569,B.) JP,54-92632,A, JP,56-79616,A, JP,56-77272,A, JP,56-7776,A, JP,56-7710,A, JP,56-20330,A, JP,63-24968,B.

[0004]Use is presented with such fair cosmetics and external preparations with goods gestalten, such as cream, a lotion, a milky lotion, a pack, face toilet, an ointment, and cataplasms, they control the melanin generation which was excellent in all, and are used as the cosmetics which do a fair effect so thru/or external preparations. In order to prevent pigmentation, such as a stain and a freckle, being promoted by ultraviolet rays, the ultraviolet ray absorbent was suitably blended with said cosmetics thru/or external preparations.

[0005]However, nevertheless, since the skin got damaged, inflammation was caused and it was accompanied by use top pain when put to ultraviolet rays for a long time, development of the quick-acting fair external preparations which have the outstanding anti-inflammatory activity was desired. kojic acid is known as an ideal milky skin agent having anti-inflammatory activity -- **** (JP,58-34446,B) -- as an effect of improving the inflammation of the critical skin, it is still insufficient, and a fair operation is also a delayed effect.

[0006]

[Problem(s) to be Solved by the Invention]Then, the purpose of this invention is to provide the skin external preparations in which it excels in anti-inflammatory activity, and a fast-acting fair operation is shown.

[0007]

[Means for Solving the Problem]By proposing this invention in order to attain said purpose, and using an extract of specific vegetation together to skin external preparations containing kojic acid and/or its derivative, The anti-inflammation effect of having excelled by both synergy is completed based on knowledge acquired by this invention person that not only ***** but a fast-acting fair effect was acquired.

[0008]According to this invention, namely, kojic acid and/or its acid derivative, and *Centraria Islandica*, *Iris*, a chebulae fructus bark, *Fumaria officinalis*, a gardenia, *Nuphar japonicum*, a euphrasy, A linden, a field horsetail, a SEIYOU mistletoe, a mallow, *Geum japonicum*, Skin external preparations excellent in anti-inflammatory activity and a fair operation containing a kind of an extract of vegetation chosen from a group which consists of *Aurantii nobllis* pericarpium, DC, an elm, a grape, *Sapindus mukurossi*, a melilot, a cornflower, and creeping saxifrage, or two sorts or more are provided.

[0009]

[Detailed Description of the Invention]As kojic acid (5-oxy-2-oxymethyl gamma-pyrone) used in this invention, What extracted kojic acid from the concentrate of the pure article of a 5-oxy-2-oxymethyl gamma-pyrone, the fermentation liquid which uses as the main ingredients the kojic

acid produced by cultivating the publicly known strain which has kojic acid productivity, and this fermentation liquid, and this fermentation liquid, and was crystallized is used.

[0010]As a kojic acid derivative, for example JP,60-10005,B, What was indicated by JP,1-45472,B and JP,3-74229,B, Or by combining sugars with the esterification material of kojic acid and the $-CH_2$ OH radical of the 2nd place of kojic acid which are indicated by JP,58-

22151,B and JP,58-22152,B, Publicly known things, such as a kojic acid derivative which stabilized the kojic acid molecule, can be used combining independent or two sorts or more.

[0011]The following can be illustrated as a raw material of the specific vegetable essence used together with kojic acid and/or its acid derivative.

[0012]Centraria Islandica (Cetraria Islandica) is a lichen and is seen in the foot district of the Alps in Germany, Switzerland, SURANSU, Spain, Tyrol, and Scandinavia. As the extract (Iceland Moss Extract), what was extracted from the entire plant can use it conveniently.

[0013]Iris florentina (Iris florentina L.) is a perennial herbaceous plant book of South Europe native Iridaceae, and as the extract (Orris Root Extract), The extract produced from a rhizome by extracting by ethanol, a 1,3-butylene glycol, purified water, or such mixtures can use it conveniently.

[0014]As a chebulae fructus bark extract (Oak Bark Extract), the extract from the bark of chebulae fructus (Cortey quercus) can use it conveniently.

[0015]Fumaria officinalis (Fumaria officinalis) is wild grass, and is seen anywhere [, such as a field, a barren area, and a roadside,]. It grows in the Temperate Zone of Europe except a northern part, and Asia and North Africa. As the extract (Fumitory Extract), what was extracted from the leaf and the flower can use it conveniently.

[0016]A gardenia (Gardenia jasminoides Ellis.) is an evergreen shrub grown wild or planted in the southwest part warm district in Japan. The extract produced from the fruits (gardeniae fructus) of a gardenia or its species of the same genus as the extract (Gardenia Extract) by extracting in purified water, ethanol, 1,3-butylene glycols, or such mixtures can use it conveniently.

[0017]Nuphar japonicum (Nuphar japonicum DC), The extract obtained from the rhizome of KOJIHONE or its species of the same genus by extracting by the 1,3-butylene glycol as the extract (Nuphar Extract) by the perennial herb of Nymphaeaceae which grow wild in a ground, a marshy place, etc. can use it conveniently.

[0018]A euphrasy (Euphrasia officinalis) is a 10 thru/or 20 general cm [in overall length] small first grader's vegetation in the Europe whole country, and is grown to a pasture, a forest, the dry hilly country, and a mountain range. As the extract (Euphrasia Extract), the extract of a leaf can use it conveniently.

[0019]As a linden extract (Tillaceae Extract, Linden Extract), From the flower or leaf of a linden (Tilia sylvestris L., Tilia cordata Mill., or Tilia europaea) to purified water. The extract produced

by extracting by propylene glycol, 1,3-butylene glycols, or such mixtures can use it conveniently. what extracted the oil-soluble extract from the flower or the leaf with sunflower oil -- it can be used conveniently.

[0020]A field horsetail (*Equisetum arvense* L.) is perennation Pteridophyta belonging to Equisetales, is widely distributed over the Temperate Zone of the Northern Hemisphere, and is seen nationally even in Japan. As the extract (Horsetail Extract), what was extracted with purified water, ethanol, propylene glycol, a 1,3-butylene glycol, etc. from the entire plant can use it conveniently. What was extracted with sunflower oil as the oil-soluble extract can use it conveniently.

[0021]A SEIYOU mistletoe (*Viscum album* L.) is the vegetation of Loranthaceae which grow wild in Europe, and what was extracted from the branch, the leaf, and the treetop can use it conveniently as the extract.

[0022]A mallow (*Malva sylvestris*) is the vegetation of Malvaceae called a common mallow, and is grown mostly in Europe. What is ethanol, propylene glycol, a 1,3-butylene glycol, purified water, etc., and was produced from the leaf or the flower by extracting as the extract (MallowExtract) can use it conveniently.

[0023]*Geum japonicum* (*Geum japonicum* Thub.) is a perennial plant of Rosaceae which grow wild in Yamano's swamp, and the extract of a leaf can use it conveniently as the extract (Avens Extract).

[0024]*Aurantii nobllis pericarpium* (*aurantii nobllis pericarpium*) is the pericarp of a mandarin orange (*Citrus unshiu* Markovich, *Citrus aurantium* L.subsp.nobilis Makino). As CHIMPIEKISU (*Citrus Unshiu Peel Extract*), the extract extracted from *aurantii nobllis pericarpium* with ethanol or purified water can use it conveniently.

[0025]A daisy (*Bellis perennis*) is seen in Europe and Asia, and grows wild in a prairie or a grass plot. As the extract (Daisy Extract), the extract of a flower can use it conveniently.

[0026]An elm (*Ulmus campestris*) is a not less than 40-m big tree, and branching is sticking out of it near the ground surface. As the extract (Elm Bark Extract), the extract of a bark can use it conveniently.

[0027]As a grape extract (Grape Extract), the extract of the fruits of AKABUDOU (*Vitis vinifera* L.) can use it conveniently.

[0028]*Sapindus mukurossi* (*Spindus mukurossi* Gaertner) is fallen-leaves Takagi which grows wild in a warm district. The extract produced from pericarp by ethanol, purified water, etc. extracting as the extract (Mukurossi Peel Extract) can use it conveniently.

[0029]A melilot (*Melilotus officinalis*) is a herb of the Leguminosae which grows wild in Europe, and is grown in various places. What was produced from the flower or the leaf by ethanol, a 1,3-butylene glycol, water, etc. extracting as the extract (Sweet Clover Extract) can use it conveniently.

[0030]A cornflower (*Centaurea cyanus* L.) is the vegetation of Compositae, is a herb often seen in Europe, and is also called a cornflower. What is produced as the extract (Cornflower Extract) by purified water, a 1,3-butylene glycol, ethanol, propylene glycol, etc. extracting a flower can use it conveniently.

[0031]Creeping saxifrage (*Saxifrage stolonifera* Meerburg) is an evergreen perennial herbaceous plant which grows wild in Yamaai's swamp and is grown by the garden. The extract produced from the entire plant by extracting with ethanol, purified water, a 1,3-butylene glycol, etc. as the extract (Saxifrage Extract) can use it conveniently.

[0032]In this invention, the loadings of said kojic acid and/or its derivative, and a vegetable extract, Also in any in the case of cosmetics, such as cream, a lotion, a milky lotion, a pack, face toilet, and essence, and the case of using it as external preparations, such as an ointment, cataplasms, and a plaster agent, Kojic acid and/or its derivative are preferably blended for a plant extract in 0.1 thru/or 5% of the weight of the range 0.001 thru/or 10% of the weight 0.01 thru/or 10% of the weight 0.0001 thru/or 20% of the weight to the whole pharmaceutical preparation.

[0033]As there will be no restriction in particular if the skin external preparations of this invention are suitable on external use use, and mentioned previously, For example, cataplasms, a plaster agent, a paste agent, cream, ointment, aerosols, Use is broadly presented with a gestalt publicly known as drugs, such as an emulsion, a lotion, a milky lotion, essence, a pack, gel, powder, foundation, SANKEA, and bath salt, quasi drugs, and cosmetics.

[0034]Various publicly known active principles used for usual when manufacturing the external preparations of this invention, For example, carpronium chloride, cepharanthin, vitamin E, vitamin-E nicotinate, Nicotinic acid, nicotinamide, nicotinic acid benzyl, ginger tincture, Pick-me-ups, such as peripheral vasodilators, such as capsicum tincture, camphor, and menthol, Antimicrobial agents, such as hinokitiol, a benzalkonium chloride, and undecylenic acid, An animal and vegetation, such as milky skin agents, such as antiphlogistics, such as lysozyme chloride, glycyrrhizin, and allantoin, ascorbic acid, and arbutin, a placenta extract, a liver extract, and a lactic-acid-bacteria culture extract, various extracts from microorganism, etc. can be used adding suitably.

[0035]For the above-mentioned drugs, quasi drugs, and cosmetics, various additive agents, such as a publicly known moisturizer, an antiseptic, an antioxidant, an ultraviolet ray absorbent and a dispersion agent, a chelating agent, a pH adjuster, perfume, and colorant, can be used together if needed besides base ingredients, such as a publicly known active principle, a surface-active agent, oil and fat.

[0036]

[Example]Next, although the example of an experiment for an example and its effect to be

shown is given, these do not limit this invention at all.

[0037]the <example 1 of experiment> rat carrageenin edema depressant action SD system male rat (weights 180 thru/or 200g) right rear -- a leg -- 0.1 ml of 1%lambda-carrageenin after subcutaneous injection to planta hypodermic, The cream pharmaceuticals (pharmaceutical preparation which blended with the following cream-pharmaceuticals base the active principle shown in Table 1) adjusted independently promptly were applied, and the leg capacity of 3 hours after was measured.

[0038]Control was made into the group (contrast) which does not apply cream pharmaceuticals, and was measured also about the cream base excluding the active principle from cream pharmaceuticals. In the exam, after adding 100 ml of solvents to 10 g and stirring an ideal plant type at a room temperature for 3 hours, the vegetable extract evaporated to dryness was used.

$$\text{浮腫率} = \frac{\text{起炎剤注入後の足容積} - \text{実験前足容積}}{\text{実験前足容積}} \times 100$$

$$\text{浮腫抑制率} = \frac{\text{コントロール群浮腫率} - \text{薬剤処置群浮腫率}}{\text{コントロール群浮腫率}} \times 100$$

[0039]

The cream base for an examination (% of the weight)

(A) Monostearin acid Polyoxy ethylene glycol (40E.0.) 2.00 Self-emulsification type glyceryl monostearate 5.00 stearic acid 5.00 Behenyl alcohol 1.00 liquid paraffins 1.00. Glyceryl trioctanoate 10.00 Antiseptic ** Quantity Perfume Minute amount (B) 1,3-butylene glycol 5.00 Purified water ** The heating and dissolving of the ingredient belonging to a complementary (A) were carried out (oil phase), and the heating and dissolving of the ingredient belonging to the (B) ingredient were carried out independently (aqueous phase). The aqueous phase was added to the oil phase, after stirring emulsification, it cooled and the vanishing cream base was obtained.

[0040]

表1-1

併用の植物エキス		コウジ酸 濃 度 (%)	コウジ酸 グルコシド 濃 度 (%)	結 果 浮 腫 抑制率 (%)
種類 (溶媒)	濃度 ($\mu\text{g/ml}$)			
—	—	1. 0	—	2 1
—	—	5. 0	—	4 8
—	—	—	1. 0	2 0
—	—	—	5. 0	4 3
アイスランドゴケ (水)	2. 0	—	—	1 0
	5. 0	—	—	1 8
	2. 0	1. 0	—	6 6
	2. 0	—	1. 0	6 2
イリス (1, 3-ブチレ ングリコール)	2. 0	—	—	3
	5. 0	—	—	1 0
	2. 0	1. 0	—	5 5
	2. 0	—	1. 0	6 3
カシ樹皮 (水)	2. 0	—	—	1 1
	5. 0	—	—	1 6
	2. 0	1. 0	—	6 0
	2. 0	—	1. 0	5 0

[0041]

表1-2

併用の植物エキス		コウジ酸 濃 度 (%)	コウジ酸 グルコシド 濃 度 (%)	結 果 浮 腫 抑制率 (%)
種類 (溶媒)	濃度 ($\mu\text{g/ml}$)			
カラクサケマン (水)	2. 0	—	—	1 2
	5. 0	—	—	2 7
	2. 0	1. 0	—	7 1
	2. 0	—	1. 0	6 8
クチナシ (水:エタノール = 1 : 1)	2. 0	—	—	1 0
	5. 0	—	—	2 1
	2. 0	1. 0	—	6 3
	2. 0	—	1. 0	6 0
コウホネ (1, 3-ブチレ ングリコール)	2. 0	—	—	9
	5. 0	—	—	2 0
	2. 0	1. 0	—	6 0
	2. 0	—	1. 0	5 7
コゴメグサ (水)	2. 0	—	—	1 1
	5. 0	—	—	2 0
	2. 0	1. 0	—	6 6
	2. 0	—	1. 0	6 1

[0042]

表1-3

併用の植物エキス		コウジ酸 濃 度 (%)	コウジ酸 グルコシド 濃 度 (%)	結 果 浮 腫 抑制率 (%)
種類 (溶媒)	濃度 ($\mu\text{g/ml}$)			
シナノキ (プロピレングリ コール)	2. 0	—	—	1 0
	5. 0	—	—	2 1
	2. 0	1. 0	—	6 8
	2. 0	—	1. 0	6 3
スギナ (エタノール)	2. 0	—	—	1 3
	5. 0	—	—	1 8
	2. 0	1. 0	—	5 7
	2. 0	—	1. 0	5 3
セイヨウヤドリギ (水)	2. 0	—	—	9
	5. 0	—	—	1 8
	2. 0	1. 0	—	6 4
	2. 0	—	1. 0	6 4
ゼニアオイ (プロ ピレングリコール : 水 = 1 : 1)	2. 0	—	—	1 3
	5. 0	—	—	2 6
	2. 0	1. 0	—	7 7
	2. 0	—	1. 0	7 5

[0043]

表1-4

併用の植物エキス		コウジ酸 濃 度 (%)	コウジ酸 グルコシド 濃 度 (%)	結 果 浮 腫 抑制率 (%)
種類 (溶媒)	濃度 ($\mu\text{g/ml}$)			
ダイコンソウ (水)	2. 0	—	—	9
	5. 0	—	—	1 7
	2. 0	1. 0	—	5 9
	2. 0	—	1. 0	5 7
チンピ (エタノール)	2. 0	—	—	7
	5. 0	—	—	1 5
	2. 0	1. 0	—	6 0
	2. 0	—	1. 0	6 1
デイシー (水)	2. 0	—	—	1 6
	5. 0	—	—	2 6
	2. 0	1. 0	—	7 7
	2. 0	—	1. 0	7 2
ニレ (水)	2. 0	—	—	9
	5. 0	—	—	2 2
	2. 0	1. 0	—	5 9
	2. 0	—	1. 0	5 9

[0044]

表1-5

併用の植物エキス		コウジ酸 濃 度 (%)	コウジ酸 グルコシド 濃 度 (%)	結 果 浮 腫 抑制率 (%)
種類 (溶媒)	濃度 ($\mu\text{g/ml}$)			
ブドウ (水)	2. 0	—	—	9
	5. 0	—	—	1 8
	2. 0	1. 0	—	6 1
	2. 0	—	1. 0	6 3
ムクロジ (エタノール)	2. 0	—	—	2 9
	5. 0	—	—	4 0
	2. 0	1. 0	—	8 0
	2. 0	—	1. 0	7 9
メリロート (1, 3-ブチレ ングリコール)	2. 0	—	—	1 1
	5. 0	—	—	2 3
	2. 0	1. 0	—	7 2
	2. 0	—	1. 0	7 6
ヤグルマギク (プロピレングリ コール)	2. 0	—	—	6
	5. 0	—	—	1 3
	2. 0	1. 0	—	6 9
	2. 0	—	1. 0	6 3

[0045]

表1-6

併用の植物エキス		コウジ酸 濃 度 (%)	コウジ酸 グルコシド 濃 度 (%)	結 果 浮 腫 抑制率 (%)
種類 (溶媒)	濃度 ($\mu\text{g/ml}$)			
ユキノシタ (エタノール)	2. 0	—	—	8
	5. 0	—	—	1 9
	2. 0	1. 0	—	6 1
	2. 0	—	1. 0	5 3

It was admitted that the effect of kojic acid or its derivative and the effect of a vegetable essence were appearing in the cream pharmaceuticals of this invention synergistically so that

more clearly than the result of Table 1.

[0046]The improvement effect of pigmentation was investigated using <Example 2> guinea pig ultraviolet pigment self-possessed depressor effect yellowish-brown-color guinea pig. This result is shown in Table 2.

Using the regions-of-back skin of a test-method yellowish-brown-color guinea pig, hair clipping of the regions-of-back hair of this guinea pig was carried out by hair clipper, and also it shaved with the electric shaver. The regions of back of this guinea pig were covered with the aluminum foil which the hole of a five-place square (2.0x2.0 cm) opened, and day by day [3] were irradiated with them 4 times for 90 seconds once [1] per day by UV-B (three SE lamps, 140 mJ/cm²). From the exposure opening day, the active principle (the vegetable essence used the same thing as Example 1) shown in Table 2 was blended with the following base, and was continuously applied between 20 days of ter dice. It judged during the 20th from the 13th after the coating start. The photographic density of skin color carried out the macro-scopic judging in the judging standard, as shown below. It observed also about the days to which the curative effect was accepted simultaneously.

[0047]

The cream base for an examination (% of the weight)

(A) Monostearin acid polyoxy Ethylene glycol (40E.0.) 2.00 Self-emulsification type glyceryl monostearate 5.00 stearic acid 5.00 Behenyl alcohol 1.00 liquid paraffins 1.00. Glyceryl trioctanoate 10.00 Antiseptic 0.10 perfume Minute amount (B)1,3-butylene glycol 5.00 Purified water ** The heating and dissolving of the ingredient belonging to a complementary (A) were carried out (oil phase), and the heating and dissolving of the ingredient belonging to the (B) ingredient were carried out independently (aqueous phase). The aqueous phase was added to the oil phase, after churning emulsification, it cooled and the vanishing cream base was obtained.

[0048]Judging standard 3: Don't accept pigmentation at all.

2: Accept few pigmentation.

1: Accept the pigmentation of a degree in the middle.

0: It is not different from a control part (taking [no] a measure).

-1 : accept pigmentation stronger than a control part (taking [no] a measure).

[0049]

表2-1

有効成分	有効成分の配合量 重量 (%)																				
	比										較 例										
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
コウジ酸	0.5																				
コウジ酸グルコシド		0.5																			
アイスランドゴケ			1																		
イリス				5																	
カシ樹皮					10																
カラクサケマン						2.5															
コウホネ							5														
コゴメグサ								1													
シナノキ									0.5												
スギナ										10											
セイヨウヤドリギ											1										
ゼニアオイ												1									
ダイコンソウ													0.5								
チンピ														1							
アイシ															5						
ニレ																5					
ブドウ																	1				
ムクロジ																		1			
メリロート																			5		
ヤグルマギク																				1	
ユキノシタ																					1
効果	1	1	1	1	1	0	0	0	0	1	0	0	0	0	0	1	0	0	1	0	0
効果の発現するまでの日数	18	18	20	20	19	20	20	20	20	19	20	20	20	20	20	18	20	20	19	20	20

[0050]

表2-2

有効成分	有効成分の配合量 重量 (%)																				
	実										例										
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
コウジ酸	0.5		0.5	0.5	0.5		0.5		0.5	0.5		0.5	0.5		0.5	0.5	0.5		0.5	0.5	0.5
コウジ酸ダルゴシド		0.5				0.5		0.5			0.5			0.5				0.5	0.5		
アイスランドゴケ	1																				
イリス		5																			
カシ樹皮			10																		
カラクサケマン				2.5																	
コウホネ					5																
コゴメグサ						1															1
シナノキ							0.5													0.5	
スギナ								10													
セイヨウヤドリギ									1												1
ゼニアオイ										1											
ダイコンソウ											0.5									0.5	
チンピ												1									1
アイシ													5								
ニレ														5							
ブドウ															1						
ムクロジ																1					
メリロート																	5				
ヤグルマギク																		1			
ユキノシタ																			1		
効果	3	3	3	3	3	3	2	3	3	3	2	3	3	3	3	3	3	3	3	3	3
効果の発現するまでの日数	14	13	13	14	14	13	15	13	14	13	16	14	13	13	13	13	13	14	13	13	13

[0051]

[The example of a formula] The example of a formula of this invention is raised to below.

"Optimum dose" means the quantity from which the whole formula will be 100% of the weight among the example of a formula.

[0052]

The <example 1 of formula> cream (% of the weight)

1. monostearin acid Polyethylene glycol (40E.O.) 2.00 2. self-emulsification type glyceryl monostearate 5.00 3. stearic acid 5.00 4. behenyl alcohol 1.00 5. liquid paraffin . 10.00 6. Tori octanoic acid -- glyceryl . 10.00 7. paraoxybenzoic acid 0.20. 8. 1,3-butylene glycol 5.00. 9. Disodium edetate 0.01 10. kojic acid 1.00 11. Centraria Islandica (water extract) 0.50 12. iris (1,3-butylene-glycol extract) 0.10 13. purified water ** 6 is warmed [the quantity manufacturing method A.1 thru/or], and it dissolves.

B. 7 thru/or 13 are warmed and it dissolves.

C. Add B to A, and emulsify, agitate and cool.

D. Fill up a container with C after cooling and consider it as after-inspection products.

Direction for use and dosage optimum dose are rubbed on the face.

[0053]

The <example 2 of formula> milky lotion (% of the weight)

1. Monostearin acid Polyoxyethylene sorbitan (20E.O.) 2.00 2. tetraoleic acid Polyoxyethylene sorbitol (60E.O.) 0.50 3. lipophilic type glyceryl monostearate 1.00. 4. stearic acid 0.50 5. behenyl alcohol . 0.50 6. avocado oil 4.00 7. Tori octanoic acid -- glyceryl 4.00 8. paraoxybenzoic acid 0.20 9. 1,3-butylene glycol 5.00 10. xanthan gum 0.14 11. disodium edetate . 0.01 12. Kojic acid 4.00 13. Fumaria officinalis (water extract) 5.00 14. purified water ** 7 is warmed [the quantity manufacturing method A.1 thru/or], and it dissolves.

B. 8 thru/or 14 are warmed and it dissolves.

C. Add B to A, and emulsify, agitate and cool.

D. Fill up a container with C after cooling and consider it as after-inspection products.

Direction for use and dosage optimum dose are rubbed on the face.

[0054]

The <example 3 of formula> face toilet (% of the weight)

1. Polyoxyethylene hydrogenated castor oil (60E.O.). 8.00 2. ethanol 15.00 3. kojic acid glucoside 7.00 4. -- gardenia (water and 1:1 mixture extract of ethanol) 2.00 5. Nuphar japonicum (1,3-butylene-glycol extract) 0.50 6. paraoxybenzoic acid . 0.10 7. citrate 0.10 8. sodium acid citrate 0.30 9. 1,3-butylene glycol 4.00 10. disodium edetate 0.01 11. purified water ** 11 is agitated [the quantity manufacturing method A.1 thru/or] uniformly, and it dissolves.

B. Fill up a container with A and consider it as after-inspection products.

Direction for use and dosage optimum dose are rubbed on the face.

[0055]

The <example 4 of formula> ointment (% of the weight)

1. monostearin acid Polyethylene glycol (40E.O.) 2.00 2. self-emulsification type glyceryl monostearate 5.00 3. stearic acid 5.00 4. behenyl alcohol 1.00 5. liquid paraffin . 10.00 6. Tori octanoic acid -- glyceryl . 10.00 7. paraoxybenzoic acid . 0.20 8. 1,3-butylene glycol . 5.00 9.

disodium edetate 0.0110. kojic acid 1.0011. euphrasy (water extract) 0.1012. linden (propylene glycol extract) 0.4013. field horsetail (ethanol extract) 1.0014. purified water . ** 6 is warmed [the quantity manufacturing method A.1 thru/or], and it dissolves.

B. 7 thru/or 14 are warmed and it dissolves.

C. Add B to A, and emulsify, agitate and cool.

D. Fill up a container with C after cooling and consider it as after-inspection products.

Direction for use and dosage optimum dose are rubbed on the face.

[0056]

The <example 5 of formula> cataplasms (% of the weight)

1. polyacrylic acid 30.00 2. kojic acid . 0.50 3. SEIYOU mistletoe (water extract). 0.10 4. mallow (1:3 mixture extract of propylene glycol and water) 0.05 5. Geum japonicum (water extract) 0.05 6. sodium polyacrylate 7.00 7. aluminium chloride 0.30 8. concentrated glycerin . 20.00 9. monooleic acid sorbitan 1.0010. titanium oxide 4.0011. purified water ** 5, 9, and 11 are warmed [the quantity manufacturing method A.1 thru/or], and it dissolves.

B. 6 thru/or 8 and 10 are warmed and it dissolves.

C. Add B to A, agitate uniformly and mix.

D. Apply C to the paint after cooling and consider it as after-inspection products.

It exfoliates and direction for use and a dosage liner are applied to the affected part.

[0057]

The <example 6 of formula> baths (% of the weight)

1. Liquid paraffin 65.00 2. di-2-heptylundecanoic acid Glycerol monostearate 5.00 3. polyoxyethylene (2E.0.)

glycerol monostearate 2.00 4. polyoxyethylene (9E.0.) mono- olate 2.00 5. polyoxyethylene (3E.0.) lauryl ether 5.00 6. vitamin E 0.20 7. kojic acid monopalmitate . 2.008. Aurantii nobllis pericarpium (ethanol extract) 3.00 9. perfume 1.0010. coloring matter fine -- Quantity 11. ethanol ** The mixture solution of the quantity manufacturing method A.1 thru/or 9 is carried out.

B. 10 is added to 11 and it dissolves in it.

C. Add B to A and agitate uniformly.

D. The soft capsule was filled up with C and it was considered as after-inspection products.

Direction for use and dosage optimum dose are put into an organ bath, and a bath is taken.

[0058]

The <example 7 of formula> essence (% of the weight)

1.1% carboxyvinyl polymer solution 10.00. 2. glycerin 20.00 3. hyaluronic acid . 0.50 4. ethanol 7.00 5. kojic acid galactoside 3.00 6. kojic acid 2.00 7. -- DC (water extract) 1.00 8. -- elm (water extract) 0.209. grape (water extract) 0.1010. Sapindus mukurossi (ethanol extract). 0.0111. Melilot (1,3-butylene-glycol extract) 0.0112. purified water ** Each of ingredients of the

quantity manufacturing method above were agitated [mixing and] to homogeneity, it dissolved, and essence was manufactured.

Direction for use and dosage optimum dose are rubbed on the face.

It was checked that each skin external preparations of the examples 1 thru/or 7 of a formula are pharmaceutical preparation which has the effect of satisfying the purpose of this invention.

[0059]

[Effect of the Invention]According to this invention, they are provided by the skin external preparations which used together kojic acid and/or its derivative, and the extract of specific vegetation, and these skin external preparations, Compared with what blended kojic acid and/or its derivative independently, anti-inflammatory activity increases synergistically and there is the feature that a fair operation is revealed in fast-acting.

[Translation done.]